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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
RAO, MANJUNATH N	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 10/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/081,455	PAULSON ET AL.	
	Examiner	Art Unit	
	Manjunath N. Rao, Ph.D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *60-68 and 81-83* is/are pending in the application.

4a) Of the above claim(s) *61-64,67 and 68* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *60,65,66 and 81-83* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2-21-02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 60-68, 81-83 are now pending in this application. Claims 60, 65-66, 81-83 are now under consideration, Claims 61-64, 67-68 remain withdrawn from consideration as being drawn to non-elected invention.

Election/Restrictions

Applicant's election with traverse of Group III, Claims 60, 65-66, 81-83 in Paper filed on 7-22-04 is acknowledged. The traversal is on the ground(s) that the restriction is improper for several reasons and at best a species election would be most appropriate. In that regard applicants submits that they stand ready to elect the species "method using the sialyltransferase from *C.jejuni*". Examiner acknowledges the traversal, however, respectfully disagrees with applicant's arguments for the same. First of all it must be noted that the methods claimed does not involve the use of only a single type of sialyltransferase. Claims 61 and 62 involve the use of α 2,6-sialyltransferase leading to the formation of a specific glycocompound which is highly different from that formed by the use of the α 2,3-sialyltransferase claimed in claims 63-68. However in order to accommodate applicant's argument, Examiner has re-restricted the claims as follows,

Group I, claims 61-62 drawn to a method of sialylating a saccharide group using α 2,6-sialyltransferase of *P.damsela*, and

Group II, claims 63-68 drawn to a method of sialylating a saccharide group using α 2,3-sialyltransferase, with claims 60, 81-83 being common to both groups.

In line with applicant's argument, Examiner acknowledges that a species election is required for group II, and hereby places the requirement of species election as follows.

Species Election

This application contains claims directed to the following patentably distinct species of the claimed invention: The species are as follows,

A) A method of sialylating a saccharide group on a recombinant glycoprotein using a bacterial sialyltransferase, wherein the enzyme is a α 2,3-sialyltransferase from the bacteria *N.meningitidis*. (Claims 63-64)

B) A method of sialylating a saccharide group on a recombinant glycoprotein using a bacterial sialyltransferase, wherein the enzyme is a α 2,3-sialyltransferase from the bacteria *C.jejuni*.(Claims 65-66)

C) A method of sialylating a saccharide group on a recombinant glycoprotein using a bacterial sialyltransferase, wherein the enzyme is a α 2,3-sialyltransferase from the bacteria *Hemophilus*. (claims 67-68)

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, 60, 81-83 are generic.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicants traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Since applicants have already indicated that they stand ready to elect the group involving the use of the enzyme from *C.jejuni*, and in order to expedite the prosecution of the instant application, Examiner has concluded that applicants have elected (above) Group II and the species *C.jejuni* (claims 65-66).

The requirement for restriction is still deemed proper and is therefore made FINAL.

Claims 61-64, 67-68 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed in Paper filed on 7-22-04.

Drawings

Drawings submitted in this application are accepted by the Examiner for examination purposes only.

Sequence Compliance

Applicant is required to comply with the sequence rules by inserting the sequence identification numbers of all sequences recited within the claims and/or specification. It is particularly noted that applicants fail to provide appropriate SEQ ID NO for short amino acid sequences recited on page 3 of the specification.. See particularly 37 CFR 1.821(d).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 60 and claims 81-83 which depend therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 60 recites the phrase "bacterial sialyltransferase". It is well known in the art that there are a number of different sialyltransferases. However, since the claim does not specify as to which specific sialyltransferase must be used, the metes and bounds of the above phrase are not clear to the Examiner. Correction is required.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 60, 65, 81-83 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of sialylating a saccharide group on a recombinant

glycoprotein using the specific sialyltransferase (ST), α 2,3-ST isolated specifically from *C.jejuni*, does not reasonably provide enablement for such a method wherein any ST isolated from any bacteria are used or wherein any bacterial ST having at least a 50% amino acid sequence homology with the amino acid sequence of *C.jejuni* α 2,3-ST are used. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 60, 65, 81-83 are so broad as to encompass the use of any bacterial ST or any bacterial ST having at least a 50% amino acid sequence homology with the amino acid sequence of *C.jejuni* α 2,3-ST. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the use of extremely large number of ST enzymes broadly encompassed in the claimed method. It is well known in the art that there are different types of STs which form specific end products and thereby affect the glycosylation of the protein (see Tsuiji et al. ref AQ in Form 1449) and therefore the specification does not teach a single universal method of using any ST for glycosylation of any polypeptide. Furthermore, since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence to obtain the

desired activity requires a knowledge of and guidance with regard to which specific amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of a single ST, i.e., α 2,3-ST from *C.jejuni*. It would require undue experimentation of the skilled artisan to use any ST from any source or to make and use the polypeptides in the claimed method. The specification is limited to teaching the use of the α 2,3-ST from *C.jejuni* but provides no guidance with regard to the making of variants and mutants of the same having at least a 50% amino acid homology to the *C.jejuni* α 2,3-ST or with regard to the use of any or all other STs. In view of the great breadth of the claim, amount of experimentation required to make/use the polypeptides in the claimed method, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polypeptides encompassed by this claim.

While enzyme isolation techniques, recombinant and mutagenesis techniques are known, and it is routine in the art to screen for multiple substitutions or multiple modifications as encompassed by the instant claims, the specific amino acid positions within a protein's sequence where amino acid modifications can be made (as in claim 65) with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the

result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass the use of any or all bacterial STs and the use of any or all ST having at least 50% amino acid homology with the α 2,3,-ST of *C.jejuni,* because the specification does not establish: (A) a single universal method of isolation of any bacterial ST and a single universal method of using such ST to sialylate a glycopeptide; (B)regions of the protein structure (i.e., *C.jejuni* α 2,3-ST) which may be modified without affecting its activity; (C) the general tolerance of STs to modification and extent of such tolerance; (D) a rational and predictable scheme for modifying any amino acid residue on the ST polypeptide with an expectation of obtaining the desired biological function; and (E) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any or STs with an enormous number of amino acid modifications for use in the claimed method. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of required ST having the desired biological characteristics for the claimed method is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 60, 66, 81-83 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 60, 66, 81-83 are directed to a method of using any or all bacterial ST polypeptides including variants, mutants and recombinants. Claims 60, 66, 81-83 are rejected under this section of 35 USC 112 because the claims are directed to the method of use of a genus of polypeptides isolated from bacteria including modified polypeptide sequences, modified by at least one of deletion, addition, insertion and substitution of an amino acid residue and fragments of the same that have not been disclosed in the specification. No description has been provided of the polypeptide sequences encompassed by the claim. No information, beyond the function of the polypeptide has been provided by applicants which would indicate that they had possession of the genus of polypeptides for use in the claimed method. The specification does not contain any disclosure of the structure of all the polypeptide sequences, including fragments and variants within the scope of the genus. The genus of polypeptides claimed is a large variable genus including peptides which can have a wide variety of structures. Therefore many structurally unrelated polypeptides are encompassed within the scope of these claims. The specification discloses only a single species of the genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the genus for use in the claimed method. Therefore, one skilled in the art cannot reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 60, 65-66, 81-83 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3, 12, 19-20, 23, 28-29, 32, 45, 50-51, 59-61, 73, 80-81 of U.S. Patent No. 6,399,336. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim, because the examined claim is either anticipated by, or would have been obvious over the reference claim. See, e.g., *In re Berg*, 140 F.3d 1428,46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi* 759 F.2d 887,225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other. Claims 60, 65-66, 81-83 of the instant application and claims 1-3, 12, 19-20, 23, 28-29,

32, 45, 50-51, 59-61, 73, 80-81 of the reference patent are both directed to method of sialylating a glycoprotein using bacterial STs, specifically *C.jejuni* α 2,3-ST or any ST having a 50% amino acid homology with *C.jejuni* α 2,3-ST. The method of sialylation claimed in the instant application and in the reference patent a good number of limitations are identical to one another. The portion of the specification (and the claims) in the reference patent that supports the recited method includes several embodiments that would anticipate the method claimed in claims 60, 65-66, 81-83 herein. Claims 60, 65-66, 81-83 of the instant application listed above cannot be considered patentably distinct over claims 1-3, 12, 19-20, 23, 28-29, 32, 45, 50-51, 59-61, 73, 80-81 of the reference patent when there is specifically recited embodiment that would anticipate mainly claims 60, 65-66, 81-83 of the instant application. Alternatively, claims 60, 65-66, 81-83 cannot be considered patentably distinct over claims 1-3, 12, 19-20, 23, 28-29, 32, 45, 50-51, 59-61, 73, 80-81 of the reference patent when there is specifically disclosed embodiment in the reference patent that supports claims 1-3, 12, 19-20, 23, 28-29, 32, 45, 50-51, 59-61, 73, 80-81 of that patent and falls within the scope of claims 60, 65-66, 81-83 herein because it would have been obvious to one having ordinary skill in the art to modify claims 1-3, 12, 19-20, 23, 28-29, 32, 45, 50-51, 59-61, 73, 80-81 of the reference by selecting a specifically disclosed embodiment that supports those claims. One of ordinary skill in the art would have been motivated to do this because that embodiment is disclosed as being a preferred embodiment within claims 1-3, 12, 19-20, 23, 28-29, 32, 45, 50-51, 59-61, 73, 80-81 of the reference patent.

Claims 60, 81-82 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3, of co-pending application 10/081,456.

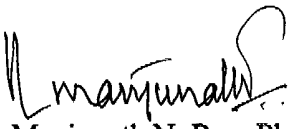
An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim, because the examined claim is either anticipated by, or would have been obvious over the reference claim. See, e.g., *In re Berg*, 140 F.3d 1428,46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi* 759 F.2d 887,225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other. Claims 60, 81-82 of the instant application and claims 1-3 of the reference application are both directed to method of sialylating a glycoprotein using STs. While the method claimed in the instant application is limited to bacterial recombinant ST it would encompass the method of use of recombinant ST3Gal1. The method of sialylation claimed in the instant application and in the reference application, a good number of limitations are identical to one another. The portion of the specification (and the claims) in the reference application that supports the recited method includes several embodiments that would anticipate the method claimed in claims 60, 81-82 herein. Claims 60, 81-82 of the instant application listed above cannot be considered patentably distinct over claims 1-3, of the reference application when there is specifically recited embodiment that would anticipate mainly claims 60, 81-82 of the instant application. Alternatively, claims 60, 81-82 cannot be considered patentably distinct over claims 1-3, of the reference application when there is specifically disclosed embodiment in the reference that supports claims 1-3, of that application and falls within the scope of claims 60, 81-82 herein because it would have been obvious to one having ordinary skill in the art to modify claims 1-3, of the reference by selecting a specifically disclosed embodiment that supports those claims. One of ordinary skill in the art would have

been motivated to do this because that embodiment is disclosed as being a preferred embodiment within claims 1-3, of the reference.

Conclusion

None of the claims are allowable.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 571-272-0939. The Examiner can normally be reached on 7.00 a.m. to 3.30 p.m. If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned is 703-872-9306/9307 for regular communications and for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.



Manjunath N. Rao, Ph.D.
Primary Examiner
Art Unit 1652

October 13, 2004